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Ayurvedic Nanomedicine (Swarna Bhasma) - Evaluation based on Analytical Parameters

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ABSTRACT

The Ayurvedic system of medicine is the treasure of metallic and mineral nanomedicines. A branch of Ayurveda, Rasashastra deals with preparation and therapeutic applications of nanomedicines. A poor scientific appraisal of Ayurvedic principles among Indian scientific community eventually resulted in a poor interdisciplinary collaboration between science and Ayurveda. Thinking of effective utilization of Ayurveda through a better understanding of its fundamentals is the recent realization. Fortunately, a few among the new genre have prompted to sense this reality and stand up as intermediaries, speaking in a mutually understandable language and retrieving the link of Ayurveda to science while keeping its original flavor intact. Bhasma form of medicine explained in Ayurveda classics has its particle size in nanometers. Swarnabhasma is such a kind of medicine which is proven to have a broad-spectrum effect especially because of its particle size. This article attempts to point out the versatile properties of Ayurvedic nanomedicine and the toxicity studies being carried out in such medicines as it is the main obstacle which stands in the way of exploring Bhasma preparations. With an inter-disciplinary approach Ayurvedic Bhasma and herbo-mineral formulations are being subjected to sophisticated analytical tests like XRD, SEM-EDX, ICP-AES etc. but still there are lacunas which needs to be addressed to find out the mechanism of action, the chemical reactions taking place in between the pharmaceutical steps adopted during the preparation of these formulations. Further researches are required on a scientific platform of Ayurveda and nanotechnology to understand the accurate properties and actions of these nanoparticles.

Key words: Nanomedicine, Swarnabhasma, Ayurveda, Rasashastra

INTRODUCTION

The Ayurvedic system of medicine is the treasure of metallic and mineral nanomedicines. A branch of Ayurveda, Rasashastra deals with preparation and therapeutic applications of nanomedicines, especially metallic and mineral nanoparticles. These metals and

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minerals are processed with various organic materials and repeated heating, and the finally prepared metal or mineral ashes are claimed to be organically structured nanoparticles. This prepared organometallic or organo-mineral nanoparticles are termed as Bhasma in Ayurveda.^[1] These preparations are reported to be safe for human use and are having various biological activities.^[2]

A poor scientific appraisal of Ayurvedic principles among Indian scientific community eventually resulted in a poor interdisciplinary collaboration between science and Ayurveda. This subsequently led to a premature demise of this thought until it has been resurrected recently with stronger evidence to rely on. Thinking of effective utilization of Ayurveda through a better understanding of its fundamentals is the recent realization. Fortunately, this realization has given rise to a spurt of an impulsive and argumentative pro-Ayurvedic generation as its eventuality.^[3] Global

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dissemination of *Ayurveda* required its scientific presentation besides minimization of its semantic barriers helping it to become comprehensible to the people exogenous to it. Fortunately, a few among the new genre have prompted to sense this reality and stand up as intermediaries, speaking in a mutually understandable language and retrieving the link of *Ayurveda* to science while keeping its original flavor intact.^[4,5]

The real significance of nanomedicine and its potential was realized only recently. Though there are many use of nano medicine, however, the primary applications of nanomedicine at present time include diagnosis of various diseases which are difficult to spot with the presently available conventional techniques in addition to crafting proficient and biosafe drug delivery systems for site specific targeting with ultimate goal of treatment of diseases.^[6] Moreover, nanomedicines can also be utilized to investigate cellular movements and molecular variations which are often related to pathological conditions with the promise of building fabricated cells, enzymes and genes.^[7] Nanomedicines can also be described as carrier systems in the nanometric scale carrying drugs, imaging agents, diagnostic agents, antibodies and others.^[8] The nanotechnology has proven to be a state of the art technology for medical scientists which enable them to reduce drug carrier size for an efficient line of attack against ailments. The foreseen enormous scientific and commercial potential of nanotechnology in the area of human health care lies in developing significantly effective medical treatment strategies.^[9] One major advantage of nanotechnology is its flexibility which enables the nanomedicines to take various shapes such as liposomes, dendrimers, nanoparticles, nanocrystals etc. so as to the meet the needs of desired or required biomedical applications.^[10]

MATERIALS AND METHODS

Swarna Bhasma (Incinerated gold)

Pharmacological actions: *Swarnabhasma* (Incinerated gold) is *Vrshya* (aphrodisiac), *Rasayana* (immunomodulator), *Hrdya* (cardiac stimulant), *Balya, Kantikara*.

REVIEW ARTICLE January 2023

Research works on Swarnabhasma as nanoparticle

- 1. Various imaging techniques were used to investigate Swarna Bhasma's (gold nanopowder) toxicity in both cancerous and noncancerous cells (HeLa and HFF-1) and to characterize its spectral properties. The results showed that gold ash particles had no impact on the cellular viability of both HeLa and HFF-1 cells, even at high concentrations or long incubation times. Moreover, it was found that the internalization level of Swarna Bhasma to cells may be improved by mechanical breaking of the large aggregates into smaller agglomerates. Hyperspectral images revealed that after breaking, the small agglomerates have different spectral properties in cells, compared to the original aggregates, suggesting that size of particles is instrumental for the subcellular interaction with human cells.^[11]
- 2. A pilot study was carried out in healthy human male participants to assess bioavailability of Swarnabhasma in three doses, viz. 30 mg plain sublingual, 30 mg oral dose mixed with black pepper powder (250 mg) and cow ghee (2.5 gm); and 240 mg oral dose mixed with black pepper powder (250 mg) and cow ghee (2.5 gm). Blood samples were withdrawn at 0, 1, 2 and 4 h after administration of dose. Estimation of gold levels in blood was carried out by inductively coupled plasma mass spectrometry (ICPMS). Results show that gold is absorbed in traces from single dose of Swarnabhasma. Maximum concentration of gold was bioavailable from 30 mg sublingual dose with Cmax 0.983 mg/L at 2 h (Tmax). Oral dose of 30 mg Swarnabhasma mixed with black pepper powder and ghee showed faster absorption with Tmax at 1 h and Cmax 0.867 mg/L, and 240 mg dose with black pepper and ghee showed Cmax 0.668 mg/L and Tmax at 2 hrs.^[12]
- The characterization of incinerated gold particles (IAuPs) in HeLa (human cells derived from cervical cancer) and HFF-1 (human foreskin fibroblast cells) in comparison to synthesized citrate-capped gold nanoparticles (AuNPs). We found that while

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REVIEW ARTICLE January 2023

individual IAuP crystallites are around 60nm in size, they form large aggregates with a mean diameter of 4711.7nm, some of which can enter cells. Fewer cells appeared to have IAuPs compared to AuNPs, although neither type of particle was toxic to cells. Imaging studies revealed that IAuPs were in vesicles, cytosol, or in the nucleus. We found that their nuclear accumulation likely occurred after nuclear envelope breakdown during cell division. We also found that larger IAuPs entered cells via macropinocytosis, while smaller particles entered via clathrin-dependent receptor-mediated endocytosis.^[13]

- 4. Acute oral administration of Swarnabhasma showed no mortality in mice (up to 1 ml /20 g b.w. of Swarnabhasma suspension containing 1mg of drug). Chronic administration of Swarnabhasma also showed no toxicity as judged by SGPT, SGOT, serum creatinine and serum urea level and histological studies. In an experimental animal model, chronic Swarnabhasma-treated animals showed significantly increased superoxide dismutase and catalase activity, two enzymes that reduce free radical concentrations in the body.^[14]
- 5. Swarna Bhasma was found to be safe at all levels tested. No significant treatment-related clinical signs were noted in all groups studied. The food and water consumption was not affected at highest given dose, i.e., 13.5 mg/kg body weight. No major alterations were observed during histopathological evaluation. Conclusion: This study indicates 13.5 mg/kg body weight as NOEL for Swarna Bhasma in Wistar rats.^[15]

Nanoparticles used in the management of Covid-19

The pandemic COVID-19 has affected more than seventy million people globally. The whole world is eagerly waiting for an effective antiviral therapy to combat COVID-19, but it is yet to be found. The emergence of COVID-19 makes imperative the need for safe and potent antiviral drugs. Many metal nanoparticles exhibit significant antiviral potential against many viral diseases. The *Ayurvedic* system of medicine is the treasure of many metal nanoparticulate drugs termed as *Bhasma*. Gold, silver, copper, zinc and iron oxide nanoparticles are effective against coronavirus. A possible mechanism of action of the metal nanoparticles against coronavirus is a disruption of outer layers of coronavirus. *Swarna Bhasma*, *Rajata Bhasma*, *Tamra Bhasma* and *Yashada Bhasma* are recommended for COVID-19 treatment due to the ability to reduce the plasma interleukins, interferons and TNF α levels.

Swarna Bhasma (incinerated gold) analyzed by X-ray diffraction (XRD) and transmission electron microscope (TEM) reveals that the size of crystallites within the Swarna Bhasma is approximately 30-60 nm.^[16] Rajata Bhasma (incinerated silver) by scanning electron microscopy (SEM) analysis shows the regular and uniform arrangement of a cluster of granules in Rajata Bhasma. The sizes of the particles range from 10 to 60 nm.^[17] The X-ray diffraction (XRD) analysis of *Tamra* Bhasma (incinerated copper) reveals that it is nanocrystalline and has a size of less than 100 nm.^[18] Lauha Bhasma (incinerated iron) shows irregular aggregates of various sizes and shapes with nanostructure on the surfaces (100-500 nm).[19] Naga Bhasma (incinerated lead) contains nanoscale structures on the surface. The width of the nanostructures lies between 30 and 50 nm, while the length ranges between 100 and 160 nm.^[20] The SEM images suggest that the Vanga Bhasma (incinerated tin) particles show granular appearance and porous morphology. These nanoparticles have spherical morphology with the size smaller than 100 nm.^[21] Particle size analysis by XRD shows that the mean particle size of Yashada Bhasma (incinerated zinc) is 49-80 nm. The particles are smooth, spherical and present in aggregates as suggested by SEM analysis.^[22]

DISCUSSION

Ayurvedic pharmaceutics are receiving a new thrust through a reappraisal of *Bhasma* preparations (preparations, where herbs, minerals and metals are incinerated to ash under supervised conditions) as novel nano-technological applications. Typical features of *Ayurvedic Bhasma* have been recently demonstrated through transmission electron Shilpa V. Rajan et al. Ayurvedic Nanomedicine (Swarna Bhasma) - Evaluation based on Analytical Parameters

ISSN: 2456-3110

REVIEW ARTICLE

January 2023

microscopy and atomic force microscopy.^[23] A further study has shown Swarna (Gold) Bhasma principally constituted of globular gold particle of 56-57 nm. Interestingly, the same study also revealed Swarna Bhasma to be devoid of any other heavy metal or organic material by its screening through Atomic Absorption Spectroscopy (AAS) and Infrared Spectroscopy (IS).^[23] This study also put to rest concerns about the presence of heavy metals in Ayurvedic preparations which otherwise clouds the popular use of Ayurvedic medicines abroad.^[24] The nano-particle size of Ayurvedic Bhasmas, has been confirmed in another study,^[25] where it is proposed that the nano-particles are responsible for its fast and targeted action. These nano-particles are proposed to be delivered to the target through rapid cellular internalization. Subsequent actions upon DNA/RNA molecule and protein synthesis within the cell are further hypothesized as possible mechanisms for rapid onset of therapeutic actions of Bhasma preparations. Pyrgiotakis (2007), with the help of Raman spectroscopy, has demonstrated the effect of Yashada (Zinc) Bhasma on intracellular DNA and proteins of the treated human lung adenocarcinoma cell line (A549)^[26] Another study found gold nano-particles (4 nm size) in increased apoptosis in B-Chronic helped Lymphocytic Leukemia (CLL). Incidentally, CLL is an disease predominantly otherwise incurable characterized by resistance to apoptosis.^[27] It is observed that the nanomedical application of various drugs is proportionate to their particle size and shape. Smaller the particle, the quicker is the cellular internalization and consequent effects. It is interesting to reiterate here that the pharmacological efficacy of a Bhasma preparation is largely attributed to the number and type of Puta (traditional incineration process) used in its making. Increased incinerations, therefore, are able to reduce particle size and subsequently give rise to increased efficacy to a given Bhasma^[28]

Current & Future Developments

At present there are three types of *Bhasmas*: metal based, mineral based and herbal based. In future this composition of *Bhasma* can be modified or new

composition of *Bhasma* can be introduced. The method of manufacturing of *Bhasma* can be modified or improved for better quality and nano property. Future application of this Nanomedicine, "*Ayurvedic Bhasma*" is immense in the field of healthcare and treatment. But official guidelines have to be set regarding: standardization, toxicity and safety studies, mass production issues, labeling rules, clinical studies and others.

CONCLUSION

Bhasma may be considered as nanomedicine and are free from toxicity in therapeutic doses. However, we have to reinvent this ancient science in the parameters and language of contemporary science. So proper scientific standardization of *Bhasma* should be takenup to maximize the therapeutic potential and properly designed randomized clinical trials should be done to demonstrate the efficacy. There is an urgent need for the practitioners of *Ayurveda*, scientific research institutions and the industry to work unitary to analyze the risk-benefit aspect of these herbo-mineral/metalbased medicines.

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Shilpa V. Rajan et al. Ayurvedic Nanomedicine (Swarna Bhasma) - Evaluation based on Analytical Parameters

ISSN: 2456-3110

REVIEW ARTICLE January 2023

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